# Leptin Level in Type 1 Diabetic and non Diabetic Post-puberty Overweight Iraqi Women.

**Samal Hakeem Kareem AL Jaff.**

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## Abstract:

Leptin is a circulating poly-peptide hormone (product in human *ob* gene) increased in obese individuals ,it appears that leptin decrease food intake and it play an important role in reproductive system , body homeostasis and metabolism .Significant correlation have been found between leptin and sexual hormones .

The aim of this study was to measure the level of leptin in high Body Mass Index (BMI) , and its effect on estrogen and plasma glucose in healthy and diabetic overweight post-puberty women ,as far as we know that there is no such data comparing leptin ,estrogen and plasma glucose in healthy and diabetic women in Iraq .We divided our study subjects into three groups: First, 20 more than 30 kg/ m² non-diabetic women. Second, diabetic post-puberty women. Third,15 normal weight post-puberty women as control.

A significant correlation between leptin and BMI ,estrogen and plasma glucose (increasing) $P<0.05$ between overweight and control normal weight women. Significant difference $P<0.05$ also found between diabetic and healthy overweight women in plasma glucose (increased), as well as a non significant differences $P<0.05$ has found between diabetic and healthy overweight women in leptin and estrogen levels.

In conclusion: leptin goes hand by hand with BMI . Leptin cause an increase in estrogen and plasma glucose in diabetic and non diabetic overweight women comparing with normal weight women.

**Key words:** Leptin , Estrogen , Overweight , Iraqi Women.

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# مستوى هرمون اللبتين في النساء العراقيات البدينات المصابات وغير المصابات بالسكري نوع ١ بعد سن البلوغ .


## الخلاصة:

اللبتين عبارة عن هرمون متعدد الببتايد يفرز من النسيج ألدهني عن طريق *ob* جين ،يزداد مستواه في دم الأشخاص البدينين ، يسبب هذا الهرمون قلة في استهلاك الطعام ويلعب دورا مهما في التكاثر والتوازن الجسمي وفي الأيض ، يعتقد وجود ترابط معنوي بين مستوى اللبتين و الهرمونات الجنسية.

إن الهدف من هذه الدراسة هو معرفة مستويات هرمون اللبتين في النساء العراقيات اللواتي يعانيين من البدانة ( لديهن مستوى عالي من BMI ) ويعانيين من السكري أيضا ومعرفة تأثير ارتفاع اللبتين على مستوى الهرمون الأنثوي (Estrogen) ومستوى سكر الدم،ولا توجد حسب علمنا دراسة تقرن بين النساء اللواتي يعانيين من البدانة أو البدانة والسكري معا في العراق.

قسمت هذه الدراسة إلى ثلاث مجموعات :الأولى/مكونة من ٢٠ امرأة بالغة مصابات بالبدانة فوق ($30\ kg/m^2$) الثانية/مكونة من٢٠ امرأة بالغة مصابة بالبدانة فوق ($30\ kg/m^2$) والسكري معا .الثالثة/ ١٥ امرأة طبيعية (مجموعة سيطرة).

وجد ارتفاع معنوي على المستوى $P<0.05$ بين المجموعة الأولى والثانية بين هرمون اللبتين والهرمون الأنثوي (Estrogen)مسببا ارتفاع الأخير،كذلك وجدت فروق معنوية على المستوى$P<0.05$ بين المجموعة الأولى والثانية في مستوى سكر الدم ،لا توجد أي فروق معنوية على المستوى $P<0.05$ في مستوى اللبتين والهرمون الأنثوي (Estrogen)بين المجموعة الأولى والثانية.

بالنتيجة فان ارتفاع مستوى هرمون اللبتين يوازي ارتفاع البدانة BMI وان هرمون اللبتين يسبب ارتفاعا في مستوى الهرمون الأنثوي(Estrogen) ومستوى سكر الدم في النساء البالغات اللواتي يعانيين من البدانة أو يعانيين من البدانة والسكري معا ، بالمقارنة مع النساء الطبيعيات.


**الكلمات المفتاحية:** لبتدن استروجين، زيادة الوزن، النساء العراقيات.

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## Introduction :

Leptin is a single-chain protein expressed by the *ob* gene, is synthesized predominantly in adipocytes, and plays an important role in the regulation of body weight ( fat storage level) ( 1,2). Leptin acts on the central nervous system, in particular the hypothalamus, suppressing food intake and stimulating energy expenditure (3).

Significantly elevated serum leptin levels are found in a considerable proportion of obese persons, implying resistance to endogenous leptin in human obesity (4). Serum leptin is a useful biomarker that reflects total body fat over a wide range of Body Mass Indexes (BMIs) (5).Obese individuals, however, often have increased leptin concentrations (6), and leptin administration shows only very limited effects (7). Recent data have indicated that this is likely the result of desensitization for the leptin signal, a phenomenon now often referred to as leptin resistance. This may occur on at least two distinct levels: saturable transport of leptin across the blood–brain barrier and abnormalities in the extent of leptin receptor activation (8).

Obesity and diabetes often go hand by hand , an association between adiposity and insulin resistance has been reported in adults and children(9). Weight loss is associated with a decrease in insulin concentration and an increase in insulin sensitivity in adults (10) and adolescents (11). In a study of 122 adolescents, obese individuals were significantly more insulin resistant and insulin resistance varied directly with the degree of adiposity and leptin levels (11).

Leptin known to play a dual role in terms of metabolism and insulin signaling, both insulin sensitizing as well as insulin antagonizing (13) . Most data available support leptin as a central satiety hormone that acts as an insulin-sensitizing factor to regulate appetite and energy balance of the body, but on the other hand it is well supported that hyperleptinemia in the presence of obesity is associated with insulin resistance in tissues such as liver, fat, and pancreatic beta-cells and muscle (14), leptin levels are negatively correlated with insulin sensitivity and T2D (15) .

The general decline in circulating estrogen levels in females has profound physiological consequences, including dramatic changes in metabolism that result in altered body fat distribution with risk of diabetic syndrome (16).

Another such hormone affecting both reproduction and feeding is leptin. Rodents without an active form of leptin are usually hyperphagic, obese and infertile (17). In human, females with low circulating leptin levels, menstruation does not occur (18).

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Because it turns out that estrogen is having a lot of signaling effects in the hypothalamus that identical to leptin ,estrogen and leptin appear to show a great deal of similarity (19 ),and because leptin and insulin work together in specific neurons in the hypothalamus region of the brain ( 8) .It has been decided to study their effect together (leptin , estrogen on plasma glucose) in obese normal and diabetic woman and the effect of high level of leptin on fertility .As far as we know that there is no available data investigating high leptin on estrogen with/without diabetes in woman.

## Materials and Methods:

Blood where collected in Al-Nu´mman Hospital (for 3 months) from obese fasting post-puberty woman ,to detect the levels of leptin , glucose and estrogen .Age, weight and length were taken to calculate the Body Mass Index (BMI) ,all patients whose BMI over 30 have been tested. We divided the subject into three groups.

1) Group A : 20 Overweight non diabetic women.
2) Group B : 20 Overweight diabetic women.
3) Group C : 15 Normal weight ,non diabetic women (control) .

BMI, leptin, glucose and estrogen were measured according to the procedure in the kit of each.

- Leptin Test : Leptin (Sandwich) ELISA. Legal Manufacture :DRG Instruments GmbH .Germany.
- Estrodiol Test : ESRADIOL (E2) Enzyme Immunoassy Test Kit .Catalog/ Number : BC-1111 . BioCheck . Inc.
- Glucose Test : We put 1ml of solution with 10 micro liter patient's serum and being left for 5 min in room temperature then read by spectrophotometer at 550 wave length, according to the kit that produced by (BIOMAGRIB)®
- BMI : Was calculated as weight in (kg) divided by squared height in cubic meter ($m^2$) ($kg/m^2$) (19).

**Statistical Analysis :**

SAS (2004) program were used to study the differences of data between groups by Least Significant Differences (LSD) test (20).

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## Results:

The differences between groups in each data of this study showed in table (1) and table(2) .In table (1) BMI had significant different $P<0.05$ between group A , group B and group C .Analysis also showed a significant differences $p<0.05$ in glucose levels between group B and both (group A and group C),no significant differences between group A and group C .

**Table (1): Shows the BMI and Plasma Glucose in Group A ,B and C**

| | BMI( kg/ m²) | | | Plasma Glucose (m mole/l) | | |
|---|---|---|---|---|---|---|
| Group | A | B | C | A | B | C |
| No.1 | 30.5 | 30 | 26.9 | 6.5 | 8.7 | 5.1 |
| 2 | 30.1 | 32.4 | 27.8 | 4.5 | 16 | 4.4 |
| 3 | 30.5 | 30.8 | 25 | 3.1 | 10.6 | 4.8 |
| 4 | 32.4 | 32.4 | 23 | 3.8 | 18 | 3.5 |
| 5 | 30.5 | 32 | 22 | 4.6 | 17.8 | 3.3 |
| 6 | 30.8 | 34.7 | 22 | 5 | 8.6 | ٢ |
| 7 | 30 | 32.7 | 20 | 4 | 16.2 | 2.6 |
| 8 | 32.9 | 35.3 | 19 | 3.5 | 11.6 | 4.5 |
| 9 | 30.5 | 34.7 | 22 | 5.5 | 8.4 | 5.8 |
| 10 | 34.6 | 30.1 | 25 | 3.5 | 19.5 | 3.6 |
| 11 | 30 | 32.2 | 26 | 5.6 | 12.4 | 3 |
| 12 | 30.1 | 34.3 | 25 | 4.7 | 11 | 4 |
| 13 | 31.4 | 32 | 23 | 6 | 9 | 4.2 |
| 14 | 31.5 | 35.3 | 20 | 4 | 11 | 3.2 |
| 15 | 30.1 | 36.3 | 20 | 4.8 | 14.8 | 3.1 |
| 16 | 33.9 | 36 | - | 3.8 | 16 | - |

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| | | | | | | |
|---|---|---|---|---|---|---|
| 17 | 31.2 | 36.1 | - | 4.5 | 9.8 | - |
| 18 | 32.8 | 37 | - | 5.5 | 10 | - |
| 19 | 30 | 34 | - | 6.5 | 9 | - |
| 20 | 31.6 | 32 | - | 4.8 | 16 | - |
| * | 31.27± 0.30 b | 33.51± 0.47 a | 23.11± 0.70 c | 5.66± 0.22 b | 12.73± 0.82 a | 3.81± 0.26 c |
| ** | 1.397 | | | 1.557 | | |

* Mean ± SE. / Different letter means significant differences P<0.05 between groups in each item.

** LSD = Least Significant Differences.

- BMI=Body Mass Index.
- Group A= 20 Overweight non diabetic women.
- Group B= 20 Overweight diabetic women.
- Group C= 15 Normal weight ,non diabetic women (control).

In table (2) estrogen data showed significant difference P<0.05 between group C and both (group A and group B),no significant difference between group A and group B in estrogen level. Leptin hormone significantly differ P<0.05 between both(group A and group B)with group C; no significant differences between group A and group B in leptin levels.

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**Table (2): Shows the Estrogen level and Leptin level in Group A ,B and C**

| | Estrogen (µg/ml) | | | Leptin (ng/ml) | | |
|---|---|---|---|---|---|---|
| Group | A | B | C | A | B | C |
| No.1 | 24 | 12.1 | 10 | 22.3 | 21.3 | 12.8 |
| 2 | 45 | 20.4 | 9 | 21 | 32.1 | 7.6 |
| 3 | 46 | 17 | 11.5 | 29.6 | 22.4 | 22.3 |
| 4 | 13.6 | 23.4 | 16 | 16.7 | 12 | 33.7 |
| 5 | 27.6 | 42.7 | 14 | 32.1 | 15.5 | 23.6 |
| 6 | 48.7 | 21.8 | 13 | 62.1 | 24.9 | 19.8 |
| 7 | 15 | 33 | 22 | 12.2 | 22.2 | 11.9 |
| 8 | 55 | 15 | 17 | 12.3 | 25.5 | 18.6 |
| 9 | 19 | 38.7 | 18 | 21.4 | 51.3 | 22 |
| 10 | 25 | 12 | 14.6 | 14 | 22 | 25 |
| 11 | 20 | 22.9 | 12 | 22 | 24.3 | 26 |
| 12 | 29.9 | 15 | 10 | 15 | 27.4 | 22 |
| 13 | 23.8 | 21.6 | 11 | 50.7 | 33.9 | 19 |
| 14 | 24 | 12.2 | 12.8 | 22 | 16.2 | 11 |
| 15 | 20 | 12.6 | 8.9 | 32.2 | 24.7 | 13 |
| 16 | 13 | 24.4 | - | 27.8 | 17.7 | - |
| 17 | 21 | 17.3 | - | 24.2 | 23.3 | - |
| 18 | 15 | 20 | - | 31.2 | 30 | - |
| 19 | 21 | 22 | - | 42.4 | 31 | - |
| 20 | 19 | 19 | - | 31 | 20 | - |
| * | 24.28± 3.08 | 21.18± 1.89 | 13.32± 0.95 | 17.64± 3.34 | 16.79± 3.03 | 10.75± 2.30 |

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| | | | | | | |
|---|---|---|---|---|---|---|
| | a | a | b | a | a | B |
| ** | 6.667 | | | 8.763 | | |

* Mean ± SE. / Different letter means significant differences P<0.05 between groups in each item.

** LSD = Least Significant Differences.

●Group A= 20 Overweight non diabetic women.

●Group B= 20 Overweight diabetic women.

●Group C= 15 Normal weight ,non diabetic women (control).

## Discussion :

The significant differences in leptin levels between both (group A and Group B) in accordance with group C , is due to high BMI level in group A and group B comparing with control C serum leptin is a useful biomarker that reflects total body fat over a wide range of Body Mass Indexes (BMIs) (5) which mean that they have more adipose tissue which can secret leptin hormone .Leptin is synthesized and secreted by adipose tissue (٢١), elevated plasma leptin levels correlated positively with total fat mass (15).

High level of estrogen in group A and group B which significantly higher than group C may be due to high level of leptin hormone appeared in those groups; leptin hormone interferes with sex hormones .In human females who have low leptin, menstruation dose not accure (١٨).Leptin maintains energy homeostasis and control reproduction by regulating the hypothalamus gonadaotropin – releasing hormone GnRH(Gonadaotropin Releasing Hormone) neuroscretory system which mainly controls the reproduction axis (٢٢),injection of leptin into *ob/ob* mice increase weight of the uterus and ovaries and number of follicles (23) ; this indicates that leptin is not only involved in energy metabolism but also may have stimulatory effects on reproduction function ,leptin is expressed in pre-ovulatory granulosa and cumulus cells in the human ovary (24).

Kitawaki; et al (25) indicate that leptin stimulates estrogen– producing activity by increasing *P 450arom* mRNA ;P450 arom protein expressive and arometese activity by

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its direct action on human luteinized arenulosa cells. Leptin further arrangeing estrogen production which is stimulated by FSH(finical stimulating hormone) and/or IGF-I which have been known to be predominant stimulators of aromatize.

Normally leptin improves insulin resistance and hypoglycemia, it also regulates lipid and glucose metabolism and insulin action independently of its effects on food intake (26).Leptin stimulates fate acid oxidation and glucose uptake in skeletal muscle (27), and inhibits glucose output and lipogenesis(28).In this study the excessive leptin in group A and group B cause increase in glucose levels that is because chronic leptin over secretion in those overweight women cause saturation of leptin receptor with time which cause a clinical case called Leptin Resistance (8) ,clearly leptin decreases food intake and insulin resistance but high level overweight old women cause leptin resistance .Leptin shown to inhibit glucose – stimulated insulin secretion in isolated islets from *ob/ob* (29), similarly high physiological increase in plasma leptin levels inhibited glucose –stimulated insulin secretion in conscious rats(30).Significantly differences between group A and group B might be because of diabetic history in group B which leads to hyperglysemia in blood.

Conclusion: These data suggest that chronic overweigh (high BMI) in women cause increase in leptin level, increase in estrogen levels and blood glucose long time under the effect of excessive leptin hormone in diabetic and healthy obese cases .

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